REMARKS

A. Regarding the Amendments

Claim 8 has been cancelled. Claims 1, 4, 5, 10, 11 and 20 have been amended as set forth in the attached "Version With Markings To Show Changes Made." As amended, the claims are supported by the specification and the original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendment is respectfully requested. Thus, upon entry of the amendments, claims 1 to 7, 10 to 13 and 15 to 20 will remain pending.

B. Rejection Under 35 U.S.C. § 112

Applicants respectfully traverse the rejection of claims 5 to 7 and 10 to 14 under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 17 that claims 5 to 7 and 10 to 14 are directed to crystallization of L-aspartic acid from a suspension cooled to between 20°C and 100°C. It is the Examiner's position that crystallization in this temperature range is not supported in the specification and that, specifically, crystallization would be unlikely to occur at temperatures higher than 50°C.

The Examiner's attention is respectfully drawn to the specification at page 19, where it is stated that:

"The fumaric acid liquid is cooled to preferably 25°C or more, more preferably 30°C or more, preferably 100°C or less, more preferably 80°C or less, most preferably 60° or less. After completion of this cooling, the liquid is preferably retained at that temperature for 1 minute to 1 hour to thereby complete the deposition of L-aspartic acid crystals."

In the claimed invention, fumaric acid is added to an ammonium L-aspartate solution, in which L-aspartic acid and a small amount of fumaric acid dissolve by forming a pairing salt with an ammonium ion. This dissolution results in a mixture. Since the ammonium L-aspartate solution is heated to a temperature within the range of 50°C to 130°C and a shearing force is applied to the mixture in the invention of claim 1 to obtain a homogenous solution, all of the added fumaric acid is dissolved (for example, the solubility of fumaric acid is 9.8g/100ml at 100°C (JIKKEN KAGAKU BINRAN p188-189, 1990 KYORITSU SHUPPAN CO., LTD., attached hereto as Exhibit A)). In the invention of claim 10, the ammonium L-aspartate solution is also heated to a temperature within the range of 50°C to 130°C. As set forth above, the heating step brings the solution to a temperature of from 50°C to 130°C. Therefore, the specification teaches that the solution is then cooled from that range to the 20°C to 100°C range. It is therefore submitted that there is support in the specification for cooling a solution into the 20°C to 100°C range for crystallization of L-aspartic acid from a cooled suspension.

It is the Examiner's allegation that "at temperatures higher than about 50°C, it appears unlikely that crystallization would occur." Applicants respectfully disagree. In the homogenous solution of claim 1 and the mixture of claim 10, the amount of ammonia, which neutralizes the added and dissolved fumaric acid, is less in the mixture (see, for example, specification page 16, lines 22-25). As a result, ionization equilibrium occurs by a salt exchange reaction between L-aspartic acid and fumaric acid based on degree of dissociation. L-aspartic acid, which dissolves by forming a pairing salt with an ammonium ion is deprived of the ammonium ion by fumaric acid. Since the solubility of L-aspartic acid in the form of an acid decreases remarkably, L-aspartic acid begins to deposit as L-aspartic acid crystals at a temperature of 50°C or more.

Additionally, in the Examples of the invention, L-aspartic acid crystals are shown to deposit at temperatures higher than 50°C. The Examiner's attention is respectfully drawn to

Examples 3, 4, 5, 6, 8 and Comparative Example 2. In all of these Examples, a combination of decreasing pressure and dropping temperatures is used to achieve crystallization. However, crystallization begins long before the temperature drops to 50°C. It is noted that on page 38 of the specification, in example 3, it is stated that, "[i]n this course, L-aspartic crystals begin to deposit at around 83°C of the liquid temperature." Similarly, in example 5 on page 43, it is stated that 1 kg of fumaric acid added to and dissolved in a 95°C solution and the solution is agitated for 3 minutes, "[t]hen, L-aspartic acid crystals began to deposit." In this example, the crystals are depositing while the solution is still at 95°C. It is noted that in many of these examples temperatures are brought to approximately 78°C and then dropped further. However, crystallization has started by the time the solution has reached 78°C. Additional support may be found in the specification at pages 17 to 18.

It is respectfully submitted that the specification does in fact provide support of a cooling range of 20°C to 100°C and that examples are given where crystallization begins at a temperature higher than 50°C. Therefore, claims 5 to 7 and 10 to 14 meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, removal of the rejection is requested.

Applicants respectfully traverse the rejection of claims 4, 8, 10 and 20 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter of the invention.

Specifically claim 4 is rejected as allegedly lacking antecedent basis for "mixed continuously," as there is no clear "mixing" step. It is Applicants' position that it would be clear to one of skill in the art that the mixing refers to the fumaric acid and heated ammonium L-aspartate solution. However, in order to clarify the language of the claim, claim 4 has been amended to state that "the shearing force is applied by mixing the resultant mixture continuously." This amendment is supported in the specification at, for example, page 16, lines 8-12. As amended, the claim possesses antecedent basis in the applying a shearing force of independent claim 1 and that step is further characterized by continuous mixing. Removal of the rejection is therefore respectfully requested.

Additionally, claim 8 is rejected as allegedly indefinite in that performance of "allowing to stand" is unlikely to be a continuous step. It is noted that claim 8 has been cancelled. It is therefore submitted that this rejection is now moot.

Claim 10 is rejected as allegedly lacking antecedent basis for "said resultant mixture." Applicants submit that the term "to form a resultant mixture" has been added for clarification to the end of the step requiring the addition of fumaric acid to the ammonium L-aspartate solution. Therefore the combination of the fumaric acid and the ammonium L-aspartate solution is the resultant mixture, as in claim 1. The Examiner has also indicated that claim 10 is confusing in the temperature range cited. The claimed invention includes an invention of claim 1, wherein a shearing force is utilized and an invention of claim 10, where a shearing force is not utilized. In claim 10, a crystal of L-aspartic acid is obtained at a temperature which is reached by cooling a mixture of fumaric acid and ammonium L-aspartate solution at a rate of 0.1 to 5°C/min to between 25°C and 100°C. The cooling rate can be easily calculated by operations commonly performed in a laboratory, which can be easily set up by a person skilled in the art. Such operations include, for example, a method in which the solution is cooled in a jacket, the method of cooling by deprivation of the heat of vaporization and the like (see, for example, specification page 18, lines 6-27). Removal of the rejection is therefore respectfully requested.

Similarly, the amendment to claim 10 should clarify the language of claim 11. It is submitted that it would be clear to one of skill in the art that the resultant mixture is the combination of the fumaric acid and the ammonium L-aspartate solution. It would also be clear to one of skill in the art that this is the mixture that is homogenous, as claimed by claim 11. However, claim 11 has also been amended to clarify that the mixture is homogenous before cooling.

Claim 20 is rejected as the sequence of steps in the claim is alleged to be uncertain. Applicants allege that this rejection is unclear. Claim 20 is dependent upon claim 1. Claim 1 clearly sets forth the steps of the method of the invention. Claim 1 comprises the step of allowing to stand or actively cooling. Claim 20 clarifies how the allowing to stand and/or

cooling step is performed. Support for the amendment to claim 20 may be found at, for example, page 20, lines 18-25 of the specification. Claim 20 does not add any additional steps to the invention method. As claim 20 does not add steps to the method of claim 1, but clarifies the methods contained therein, it is unclear how the sequence of steps could be uncertain in claim 20. The sequence of steps is clearly set forth in claim 1. Therefore, removal of the rejection is respectfully requested. Alternatively, clarification of the rejection is requested.

As set forth above, Applicants submit that claims 4, 8, 10 and 20 meet the definiteness requirement of 35 U.S.C. §112, second paragraph. Accordingly, removal of the rejection is requested.

C. **Rejection Under 35 U.S.C. § 103**

Applicants respectfully traverse the rejection of claims 1 to 8, 10 to 13 and 15 to 20 under 35 U.S.C. 103(a) as allegedly unpatentable over Nore et al., Brun et al., Pavia et al. and Tan et al. The Examiner states that all previous rejections are maintained and that Applicants' arguments are not persuasive. Applicants respectfully maintain their position with regard to the arguments previously set forth and assert that the claimed invention is not obvious over this combination of references, as the combination of references does not teach or suggest all of the elements of the claimed invention.

It was alleged in Paper No. 14 and is maintained in Paper No. 17 that Nore teaches a method of producing aspartic acid wherein fumaric acid is added to ammonium aspartate followed by heating and crystallization. The Examiner has alleged that the fumaric acid, when in an aqueous suspension, may potentially contain alcohol. Applicants respectfully disagree.

It is Applicants' position that the fumaric acid of the invention, when in aqueous form is in water as a solvent. Webster's Dictionary at www.webster.com defines aqueous as "of, relating to, or resembling water; made from, with, or by water." Therefore it is respectfully submitted that the "aqueous form" of the claimed invention refers to fumaric acid dissolved in water. The Examiner's attention is respectfully drawn to pages 45, 49 and 50 of the specification, where the

fumaric acid in the Examples is added in slurry form. In all three of these examples, the fumaric acid is combined with water to form the slurry. No additional solvents are used to create the aqueous suspension. In both the specification and the claims, there is no requirement or even a suggestion of alcohol for the aqueous suspension of fumaric acid. Additionally, the ammonium fumarate solution in claim 1, to which the fumaric acid is added, does not contain alcohol. In the interest of advancing prosecution, Applicants have added the language "which consists essentially of ammonium fumarate and water" to clarify the term "ammonium fumarate solution" in claim 1. Support for this amendment may be found in the specification, for example, at page 12, lines 2-11 and Table 3. Applicants therefore respectfully submit that the aqueous suspension of claim 1, prior to and after addition of fumaric acid, clearly does not comprise alcohol.

As previously noted, the alcohol is used in Nore to increase the solubility of fumaric acid in the ammonium fumarate mixture. However, no such alcoholic solvent is necessary in the claimed invention. Instead, the claimed invention discloses addition of fumaric acid in the form of dry crystals, moisture-containing crystals or an aqueous suspension to a heated ammonium L-aspartate solution (50 to 130°C) without using an alcoholic solvent. Where a solvent is used, it is water, as set forth in the Examples. Nore, in combination with Brun, Pavia, and Tan, do not teach or suggest a heated ammonium L-aspartate solution or use of water as a solvent for fumaric acid.

Additionally, by the use of water as a solvent instead of alcohol, the claimed invention has many advantages. With use of an alcoholic solvent, the solvent may cause the degeneration of the enzyme aspartase. In contrast, in the claimed invention, the aspartase is not inhibited nor deactivated by water. It is alleged in Paper No. 17 that because aspartase has thermostable properties, it may have stability in the presence of alcohol. Applicants do not understand this allegation. Thermostability and stability in the presence of alcohol are two completely diverse characteristics of an enzyme. In heating, vibration of a molecule increases as the temperature rises. As a result, the three dimensional structure of the enzyme breaks and activity decreases. Alternatively, degeneration of an enzyme by alcohol is caused by a change in structure. The hydrophilic enzyme surface which is a fundamental structure of the enzyme protein and the

hydrophobic portion which forms the catalystic center inside the enzyme are reversed and the hydrophobic portion is brought to the surface. Aspartase changes more remarkably due to alcohol than by heating. Additionally, the Examiner asserts that there is a "claim designed limitation to the effect that the reaction all occurs [sic] in the same pot..." However, it is noted that there is no description of "the same pot" in the claims of the present invention. Applicants therefore respectfully request support for the Examiner's assertion that because aspartase has thermostability, it also has stability in the presence of alcohol.

In addition, as previously set forth, there are additional aspects of the invention that Nore does not teach, either alone or in combination with Brun, Pavia, and Tan. Specifically, Nore et al. does not teach a use of water as a solvent for fumaric acid, or any solvent other than an alcoholic solvent, does not teach addition of fumaric acid to a heated ammonium L-aspartate solution, does not teach the cooling rate of the claimed invention and does not teach crystallization before filtration. It is also submitted that Nore, taken in combination with Brun, Pavia, and/or Tan, still does not teach or suggest all of the elements of the claimed invention and that the claimed invention is therefore not obvious in light of these references.

Finally, the Examiner alleges that Applicants rely on the gradual cooling process as "the crux of the invention" while the Examiner observes that this limitation is only in claims 5 and 10. Applicants respectfully disagree. The cooling period is essential to the claims of the invention and it is contained in both independent claims 1 and 10, from which all of the other claims depend. While claims 5 and 10 specify the rate of cooling, claim 1 requires that there be a shearing force applied and a cooling step in order to crystallize L-aspartic acid. However, the rate of cooling is not essential in claim 1. It is agreed that this cooling step is essential to the claimed invention, however it is Applicants' position that this requirement is adequately set forth in both of the independent claims of the invention. It is maintained that Nore and Brun do not teach a cooling step as in the claimed invention, as set forth in Applicants' response mailed June 5, 2002.

Furthermore, the crystallization of L-aspartic acid may occur by only retaining a reaction solution for 0.1 second to 1 hour upon dissolution of he fumaric acid (see, for example, specification page 16, lines 19-22). In this case, the crystallization of L-aspartic acid begins under high temperature conditions by this operation without cooling. Since the resultant mixture is a supersaturated solution due to addition of fumaric acid to the heated ammonium L-aspartate solution in a molar ratio of 0.4 to 0.8 to the total molar amount of ammonium L-aspartate and ammonium fumarate contained in the ammonium L-aspartate solution in the claimed invention, crystallization may occur easily at high temperature by a salt exchange reaction in order to resolve the instability of a supersaturated solution.

Additionally, although the crystallization of L-aspartic acid in the claimed invention occurs while cooling to 100°C, it does not mean stopping cooling at 100°C. Further cooling to a lower temperature is intended (see, for example, specification page 19, lines 12-15).

The claimed invention teaches a method of preparing aspartic acid wherein fumaric acid is dissolved in the heated ammonium L-aspartate solution and L-aspartate is crystallized under specific conditions without an alcoholic solvent, which is not taught or suggested by the cited references. Additionally, the method of the present invention can successfully produce a needle-like L-aspartic acid crystal having mainly 30-1000 μm (see, for example, specification page 19, lines 18-19). Therefore, in filtration of needle-like L-aspartic crystals of this size, liquid passes through them quickly. Thus, their purity can be improved by simple washing operations. This effect cannot be obtained in any of the cited references, nor was it taught or suggested by the cited references. As Nore et al., viewed in light of Brun et al., Pavia et al. and Tan et al. do not teach or suggest all of the elements of the claimed invention, claims 1 to 8, 10 to 13 and 15 to 20 are not obvious in light of those references. Removal of the rejection is therefore respectfully requested.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 1 to 7, 10 to 13 and 15 to 20 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Four times amended) A method for producing L-aspartic acid comprising:

treating an ammonium fumarate solution, which consists essentially of ammonium fumarate and water, with aspartase to generate an ammonium L-aspartate solution;

heating said ammonium L-aspartate solution to a temperature within the range of 50 to 130°C;

adding fumaric acid in the form of dry crystals, moisture-containing crystals, or an aqueous suspension to said heated ammonium L-aspartate solution in a molar ratio of 0.4 to 0.8 to the total molar amount of ammonium L-aspartate and ammonium fumarate contained in the ammonium L-aspartate solution to form a resultant mixture and applying a shearing force to the resultant mixture, while maintaining the temperature between 50°C and 130°C to obtain a homogenous solution;

allowing to stand and/or cooling said homogenous solution to crystallize L-aspartic acid, thereby obtaining a suspension containing L-aspartic acid; and

separating L-aspartic acid crystals from said suspension.

4. (Three times amended) The method according to claim 1, wherein said shearing force is applied by mixing the resultant mixture continuously [fumaric acid and said heated ammonium L-aspartate solution are mixed continuously].

5. (Four times amended) The method according to claim 1, wherein said cooling is performed at a rate of 0.1 [–] to 5°C/min until the temperature of said homogenous solution is brought to between 25 and 100°C.

10. (Four times amended) A method for producing L-aspartic acid comprising:

treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution;

heating said ammonium L-aspartate solution to a temperature within the range of 50 to 130°C;

adding fumaric acid in the form of dry crystals, moisture-containing crystals, or an aqueous suspension to said ammonium L-aspartate solution to form a resultant mixture; and

cooling said resultant mixture at a rate of 0.1 to 5°C/min to between 25 and 100°C, thereby obtaining a suspension containing L-aspartic acid; and

separating L-aspartic acid crystals from said suspension.

11. (Three times amended) The method according to claim 10, wherein said resultant mixture before cooling is a homogenous solution.

20. (Twice amended) The method according to claim [8] 1, wherein said allowing to stand and/or cooling is performed by feeding said homogenous solution into a crystallization slurry vessel [continuous method is performed by feeding said homogenous solution into a suspension containing L-aspartic acid].